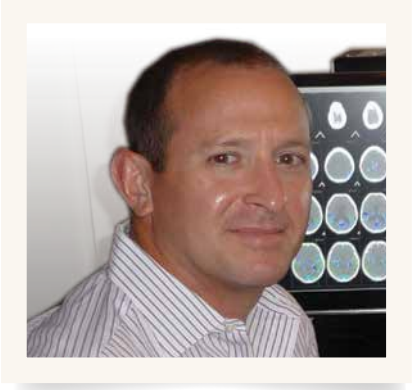
The Role of the Radiologist in Alzheimer's Disease

By Barry J. Menick, M.D.

"TRUTH DOES NOT BECOME MORE TRUE BY VIRTUE OF THE FACT THAT THE ENTIRE WORLD AGREES WITH IT, NOR LESS SO EVEN IF THE WHOLE WORLD DISAGREES WITH IT."
—MAIMONIDES, *THE GUIDE FOR THE PERPLEXED*



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THIS YEAR, I had the good fortune to attend the 50th Annual Meeting of the American Society of Neuroradiology and the 6th Annual Meeting of the American Society of Functional Neuroradiology. My objective was to focus on Alzheimer's disease. According to the 2012 annual report released by the Alzheimer's Association, 5.4 million Americans are living with Alzheimer's disease. One in eight older Americans has the disease. It is the sixth-leading cause of death in the United States. More than 15 million Americans provide unpaid care valued at $210 billion for patients with Alzheimer's disease and other dementias. Payments for care are estimated to be $200 billion in the United States in 2012.

Tremendous resources have been dedicated to the pathophysiology, diagnosis and treatment of this disease, with mixed results. It is disappointing there is no prevention, cure or treatment that will slow the ultimate progression of the disease. Those of us in the medical profession, however, need to stay focused on our individual roles in the care of these patients and their families. Our role is to diagnose Alzheimer's disease as quickly and as accurately as possible. The radiologist's toolkit now includes exciting new diagnostic imaging tools that are available today at South Texas Radiology Imaging Centers (STRIC).

Brain imaging can identify three biomarkers associated with the predementia form of Alzheimer's disease: neurodegeneration (identified via magnetic resonance imaging), hypometabolism (identified via FDG-PET) and fibrillar amyloid deposition (identified via amyloid positron emission tomography). Fluoroscopically guided lumbar puncture can be performed to identify the CSF biomarkers of tau protein elevation and beta-amyloid depression.

Patients with normal cognition and one of these biomarkers are classified as "at risk with Alzheimer's disease pathology" or as having "preclinical Alzheimer's disease." Patients with mild symptoms and one of these biomarkers are classified as having "prodromal Alzheimer's disease" or "mild cognitive impairment due to Alzheimer's disease." Patients with clinical dementia and Alzheimer's phenotype are classified as having "Alzheimer's disease dementia." Early diagnosis is essential to initiate appropriate medical therapy to preserve functional status and allow time to facilitate life planning and relationship preservation.

Magnetic resonance imaging (MRI) is the indispensable imaging modality of modern neuroradiology. Even the most experienced radiologists, however, will have difficulty characterizing the degree of cortical volume loss or ventricular enlargement in older patients due to variability. Quantitative CSF flow MRI can be used to obtain stroke volume through the cerebral aqueduct. This objective measure can identify patients with normal pressure hydrocephalus whose symptoms, including dementia, may respond to shunting.

The medial temporal lobe, the locus of early Alzheimer's pathology, is particularly difficult to characterize due to its complexity and small size. Fortunately, U.S. Food and Drug Administration (FDA)-approved MRI software enables us to objectively quantify hippocampal volumes and compare them to a normal database. This volumetric analysis is available at all STRIC MRI sites. While atrophy on MRI is the imaging manifestation of the neurodegeneration biomarker, a negative MRI study does not exclude the presence of Alzheimer's pathology. In fact, amyloid plaque can begin to accumulate in the brain 10 years or more before symptom onset.

Brain positron emission tomography (PET) generates images of fluorine uptake proportional to cortical glucose metabolism. Hypometabolism (a result of synaptic dysfunction and neuronal

loss) in characteristic distributions is another biomarker that identifies the predementia form of Alzheimer's disease. While causation is a hotly disputed topic, it suffices to say that the earliest pathologic process involves the entorhinal cortex (ERC) in the medial temporal lobe and results in a functional disconnection of the hippocampus. While atrophy of the medial temporal lobe evolves over time, neuronal dysfunction is ongoing in the network of neurons connected to the ERC.

PET can be difficult to accurately assess for early pathology. STRIC is fortunate to have FDA-approved quantitative analysis software that compares patients' FDG-PET regional uptake with that of normal cohorts. This has been an invaluable tool in increasing confidence levels and sensitivity in the detection of early Alzheimer's disease and in differentiating from frontotemporal lobe dementias. The high sensitivity and specificity of FDG-PET compared with cognitive testing and clinical assessment has led the American Academy of Neurology to modify its algorithm in the evaluation of cognitive impairment to include earlier FDG-PET scanning.

As with many new imaging modalities, it is possible to overstate the accuracy of differentiation between Alzheimer's disease and frontotemporal lobe dementias. There is some overlap between hypometabolism patterns. While the cholinesterase inhibitors used to treat Alzheimer's disease are of no value to patients with frontotemporal lobe dementia, it would be most unfortunate to make a diagnostic error that would deny a patient a chance to maintain cognition and independence for any amount of time. The FDA has recently approved Amyvid, an isotope for amyloid PET imaging that uses radioactive fluorine attached to an agent that binds amyloid plaques in the brain. The amyloid plaque is one of the pathologic substrates of Alzheimer's disease. (Tau protein in neurofibrillary tangles is another.) A positive Amyvid scan indicates moderate to frequent amyloid neuritic plaques.

Amyvid is commercially available but extremely expensive compared to FDG. The Centers for Medicare & Medicaid Services has not yet provided guidance or approval for reimbursement. How this agent will fit into our toolbox from both cost and efficacy perspectives is to be determined. Until the pathophysiology of the disease is better established, leading to effective treatment and prevention, I will continue to focus on the tools currently available to make an early and accurate diagnoses of the progressive neurodegenerative diseases.

Barry J. Menick, M.D., is a fellowship-trained diagnostic neuroradiologist with a special interest in neurodegenerative disorders. He received his medical degree from the Duke University School of Medicine in 1981. Dr. Menick completed his radiology residency and a two-year neuroradiology fellowship at the Hospital of the University of Pennsylvania in Philadelphia. He has been a senior member of the American Society of Neuroradiology since 1991. For more information, please contact South Texas Radiology Imaging Centers at (210) 319-4021, visit www.stric.com or follow STRIC on Facebook.